In the present Office Action, The Examiner has restricted the pending claims into the following six groups:

I. Claims 1-19 and 38-43, drawn to the compounds of formula I wherein X and Y are CH, R^2 is alkyl, alkenyl, haloalkyl, cycloalkyl, aryl, aralkyl, hydroxyalkyl, alkoxyalkyl, and their pharmaceutical composition, classified in class 564, subclass 374.

II. Claims 1-19 and 38-43, drawn to the compounds of formula I wherein X and Y are CH, R^2 is $NR^{13}R^{14}$, and their pharmaceutical compositions, classified in class 564, subclass 86.

III. Claims 1-19 and 38-43, drawn to the compounds of formula I wherein X and Y are CH, R^2 is alkoxycarbonylalkyl, and their pharmaceutical compositions, classified in class 560, subclass 12.

IV. Claims 1-43, drawn to the compounds of formula I wherein one of X and Y is N and their pharmaceutical compositions, classified in class 546, and respective subclasses.

V. Claims 1-43, drawn to the compounds of formula I wherein both X and Y are N, and their pharmaceutical compositions, classified in class 544, and respective subclasses.

VI. Claims 44-49, drawn to a method of using the compounds of formula I, classified in class 514, subclass 646.

Applicants are at a loss to discern which restriction and election is operative at the present time. Applicants respectfully request the clarification of the restriction requirement.

Nonetheless, Applicants traverse the above restriction based on the following arguments.

Section 803.02 of the M.P.E.P. provides:

> Since the decisions in *In re Weber* and *In re Haas*, it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility.

Compounds of the present invention all have, *inter alia*, anti-inflammatory activity; therefore, the requirement for sharing a common utility as stated in §803.02 of the M.P.E.P. is satisfied. In addition, all compounds of the present invention have an aromatic ring moiety which has a sulfonyl group and an amino group that are located para to each other. Present inventors have identified these structural features as being essential features of the utility discussed above. Therefore, the requirement for sharing a substantial structural feature for determining unity of invention is also satisfied.

Since all the requirements for the unity of invention as defined by the Court and reiterated in M.P.E.P. §803.02 are satisfied in the pending claims, Applicants submit that the Examiner's restriction requirement is improper.

Applicants further submit that the search of Group I claims will necessarily include, at the minimum, claims in Groups II and III, because they are all directed to a phenyl derivative. Furthermore, a search of a 6-membered aromatic compound having a sulfonyl and an amino substituents para to each other will include all the compounds of Groups I-V. Therefore, all the compounds of Formula I are capable of being examined together. In addition, a search of compounds of Formula I necessarily include a method for using the compound of Formula I to determine its novelty. Thus, the prior art search is not extended unnecessarily and the invention as defined by the Applicants can be examined on the merits.

At the very least, Applicants request that the election to prosecute Group 1, Claims 1-19 and 38-43 be maintained as conveyed in the telephone conversation of December 12, 2001.

Applicants specifically request that should the claims of Group I be allowable, claims 44-49 relating to a method of using the compounds of the invention be rejoined and examined in the present application. The law is clear that where product and a method of use claims are presented in the same application, rejoinder of the method of use claims is permitted when the product claim is found allowable. See M.P.E.P. §821.04; *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996); *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995).

Rejection under 35 U.S.C. §112, first paragraph

Claims 1-19 and 38-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or

use the invention. Specifically, the Examiner alleges that the scope of the term "prodrug" is not adequately enabled, because the choice of a "prodrug" will vary from drug to drug.

The first paragraph of §112 requires that the disclosure of a patent application be such that persons skilled in the art, having read the patent application, would be able to practice the inventions described by the claims. There is no legal requirement that this be done in any particular manner. An enabling disclosure can be provided by the use of illustrative examples or simply by broad terminology. *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). Moreover, a patent application must be deemed to be enabling unless there is reason to doubt the truth of statements contained in the patent application relating to making and using the invention. *Id* at 369-370.

The specification provides ample disclosure to enable one skilled in the art to make and/or use the present invention. For example, page 9, lines 10-19, of the specification provides how one can make prodrugs of compounds of the present invention. One skilled in the art will readily recognize suitable functional groups that can be modified to be cleaved *in vivo* to release the parent compound. One skilled in the art also will recognize suitable modifications which allow *in vivo* cleavage to release the parent compound. The specification provides that prodrugs include compounds in which a hydroxyl, amino or sulfhydryl group is modified to be cleaved *in vivo*. Such modification includes converting a hydroxyl group to an ester. Page 9, lines 14-19. Therefore, making and/or using the prodrugs of compounds of the present invention is enabled by the present application.

In order to make nonenablement rejection, the Examiner must provide an evidence or technical reasoning substantiating nonenablement. See MPEP §2164.04 and *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). In the instant case, the Examiner has not met the initial burden of proof to establish that the claimed invention is nonenabled.

Accordingly, Applicants respectfully submit that the rejection under 35 U.S.C. §112 is without merit and request that the rejection be withdrawn.

Rejection under 35 U.S.C. §112, second paragraph

Claim 1 stands rejected under 35 U.S.C. §112, second paragraph, allegedly for being indefinite and failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office Action alleges that the term "and" in the phrase "and prodrugs, individual isomers..." is indefinite because it is unclear whether the claim is drawn to a compound or a mixture of compound. Claim 1 has been amended by replacing the term "and" with "or" as suggested by the Examiner, thereby obviating this rejection.

In addition, the Office Action alleges that the terms "heteroaryl" and "heterocyclyl" are unclear to the array of heteroatoms, size of the rings, as well as nature of atoms as ring members. The Office Action then cites *In re Wiggins* 179 U.S.P.Q. 421 (C.C.P.A. 1973) for the proposition that these terms are indefinite.

Applicants traverse the rejection based on the following reasons.

The present application explicitly defines the array of heteroatoms, size of the rings as well as nature of atoms which constitute the ring

On page 5, lines 21-23, the specification defines "heteroaryl" as "a monovalent monocyclic or bicyclic radical of 5 to 12 ring atoms having at least one aromatic ring containing one, two, or three ring heteroatoms selected from N, O, or S, the remaining ring atoms being C. The specification defines "heterocyclyl" as "a saturated or unsaturated non-aromatic cyclic radical of 3 to 8 ring atoms in which one or two ring atoms are heteroatoms selected from O, NR,...or $S(O)_n$...the remaining ring atoms being C, where one or two C atoms may optionally be replaced by a carbonyl group" Page 6, lines 14-17. As these two definitions clearly indicate, the array of heteroatoms for "heteroaryl" and "heterocyclyl" is explicitly defined in the specification. In addition, the size of the rings as well as the nature of atoms that constitute the ring are also clearly defined.

The term "heterocyclic" in *In re Wiggins* was defined as a heterocyclic having a "group of five to seven ring atoms, from one to two nitrogen atoms, and up to one oxygen atom...." *In re Wiggins* at 422.

In contrast to *In re Wiggins*, the specification of the present invention limits the array of atoms which can be present in the ring to N, O, S, and C for "heteroaryl" and to O, NR, $S(O)_n$, C,

and a carbonyl group for "hetereocyclyl". Therefore, terms "heteroaryl" and "heterocyclyl" in the present application are clearly defined.

The Office Action also alleges that the terms "alkyl", [sic] "arylalkyl", "alkoxyalkyl", etc. recited in Claim 1 read on carbons of non-limiting length. The Office Action then cites *In re Hawkins* (C.C.P.A. 1973) for the proposition that carbon radicals of unlimited chain lengths and ring sizes are indefinite.

Applicants direct the Examiner's attention to pages 3-11 of the specification, where the number of carbon atoms for these terms are explicitly defined. For example, the term "alkyl" refers to "one to six carbon atoms" in a linear chain or "three to six carbon atoms" in a branched chain. Page 3, lines 17-18. The term "aralkyl" (incorrectly stated in the Office Action as "arylakyl") is defined as "a radical $-R^aR^b$ where R^a is an alkylene group and R^b is an aryl group...." Page 4, lines 19-20. The specification defines "alkylene" as having "one to six carbon atoms" in a linear chain or "three to six carbon atoms" in a branched chain. Page 3, lines 20-21. The specification also defines "aryl" as having "6 to 10 ring atoms". Page 4, lines 7-8. Therefore, the number of carbon atoms in "aralkyl" is clearly defined in the specification. In a similar manner, the number of carbon atoms in other terms are clearly defined.

Accordingly, Applicants submit that the rejection under 35 U.S.C. §112, second paragraph is unwarranted and request withdrawal of all the rejections under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102

Different claims stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by the cited references. It is axiomatic, that a rejection under 35 U.S.C. §102 is proper if, and only if, each and every element of the claim is found in a single prior art reference. As discussed in detail below, the cited references do not disclose every element of the present invention.

The Sebti Reference

Claims 1-4 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Sebti et al., Chem. Abstract 130:25338 (the "Sebti reference"). Specifically, the Office Action alleges that the claimed compounds read on the reference compound RN 216232-65-4.

The reference compound RN 216232-65-4 of the Sebti reference comprises methylthio (–SCH_3) moiety attached to the phenyl ring. In addition, the aromatic ring which corresponds to either "B" or R^1 of compound of Formula I comprises two substituents, a substituted phenyl ring (i.e., 2-methylphenyl) and an amide group which comprises methionine moiety (i.e., –C(O)NH–$CH(CO_2H)$–CH_2–CH_2–SMe).

Unlike the reference compound RN 216232-65-4 of the Sebti reference, compounds of the present invention are directed to an aromatic moiety comprising a sulfonyl (–SO_2R^2) moiety. The substituents on the aryl group (i.e., "B" or "R^1") are limited to those specified in the definition of "aryl". Page 4, lines 7-18. None of the possible substituent choices for aryl includes a substituted phenyl or an amide group which comprises methionine moiety.

Therefore, the Sebti reference does not disclose all of the limitations of the present invention.

The Jones Reference

Claims 1, 2, 12, 13, and 43 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Jones et al. (J. Med. Chem. [sic] 1995) (the "Jones reference"). Specifically, the Office Action alleges that the claimed compounds read on compound 35 on page 907 of the Jones reference.

The portion of compound 35 of page 907 of the Jones reference which corresponds to "B" of compound of Formula I of the present invention comprises 4-oxo-quinazolinyl moiety.

In contrast, as amended, the moiety "B" of Formula I of the present application is limited to aryl, furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl. None of these moieties corresponds to a 4-oxo-quinazolinyl moiety of compound 35 of the Jones reference.

Therefore, the Jones reference does not anticipate the present invention.

The Berman Patent

Claims 1, 2, 12, 13, and 43 also stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 4,857,530, issued to Berman et al. (the "Berman patent").

The portion of compounds of the Berman patent which corresponds to "B" of compound of Formula I comprises 4-oxo-quinazolinyl moiety

By the present amendment, the values of "B" of Formula I of the present application has been limited to aryl, furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl. None of these moieties corresponds to a 4-oxo-quinazolinyl moiety required in compounds of the Berman patent.

Therefore, compounds of the present invention are not anticipated by the Berman patent.

The Hirsch Reference

Claims 1, 2, 12-14, 16, 17, and 43 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Hirsch et al. (Chem. Abstract 11:101836) (the "Hirsch reference"). Specifically, the Office Action alleges that the claimed compounds read on the reference compound RN 89985-16-0.

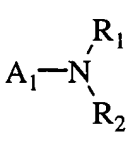
The portion of compounds discussed in the Hirsch reference which corresponds to the aryl moiety comprising a sulfonyl group in compounds of the present invention is a phenyl ring which has substituents R^3 and R^4. See the CAS report provided by the Examiner. Substituents R^3 and R^4 are limited to "H, halo, CF3, NO2, alkyl, alkoxy, alkylthio... " and do not include a sulfonyl group. See the Abstract of the CAS report.

In compounds of Formula I of the present invention, the substituent that corresponds to "R^3" or "R^4" of the Hirsch reference, is a sulfonyl group, i.e., moiety of the formula $-SO_2R^2$. Therefore, compounds disclosed in the Hirsch reference do not anticipate compounds of the present invention.

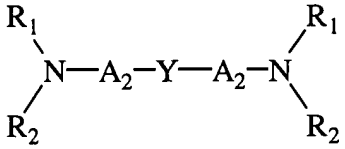
The Mattor Reference

Claims 1-4 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Mattor et al. (Chem. Abstract 86:197939) or U.S. 3,994,724 (the "Mattor reference").

The reference compounds disclosed in the copy of CAPLUS computer search report contain thiomethyl (–SMe) or thioethyl (–SEt) substituent on the phenyl ring. Specifically, the Mattor reference discloses aniline compounds corresponding to the following formulas:



[Formula A]



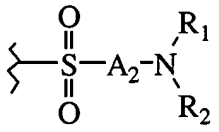
[Formula B]

wherein A_1 represents alkoxyphenyl, alkylthiophenyl, phenoxyphenyl, phenylthiophenyl, benzyloxyphenyl or benzylthiophenyl; A_2 represents phenylene or

substituted phenylene; Y represents oxo, thio, dithio or sulfonyl; R_1 represents alkyl, benzyl, and substituted benzyl; R_2 independently represents a member of R_1.

Col. 3, lines 1-15 of the Mattor reference. Thus, none of the Compounds of Formula A in the Mattor reference contains a sulfonyl substituted aromatic moiety.

Compounds of Formula B in the Mattor reference may comprise a sulfonyl substituent (where Y = sulfonyl, A_2 = phenyl or substituted phenyl and that portion of the formula can be represented by formula C below.



Formula C

The moiety $-A_2-N(R_1)(R_2)$ in Formula C, corresponding to R^2 of Formula I of the invention, is a phenyl or a substituted phenyl that is further substituted with an amino group. This amino group of the Mattor reference is further substituted with a benzyl- or a substituted benzyl- group. In contrast, substituent R^2 of the present invention is limited to "alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, or $NR^{13}R^{14}$". As shown in the definition on page 4, lines 7-19, the aryl group of the present invention does not include an aryl group having a benzylamino or a substituted-benzyl amino substituent.

Thus the compounds of the present invention are different from the specific reference compounds disclosed in CAPLUS computer search report of the Mattor reference and the compounds of Formula A of the Mattor reference.

Therefore, the Mattor reference does not disclose all the elements of the claims of the present invention.

The Okada Reference

Claims 1-5 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Okada et al. (Chem. Abstract 127:242825) (the "Okada reference"). Specifically, the Office Action alleges that the claimed compounds read on the reference compound RN 157911-86-9.

The Okada reference discusses various N,N-disubstituted-5-aminopyrimidine derivatives, including compound having RN 157911-86-9. Thus, compounds discussed in the Okada reference

comprise a pyrimidine moiety. The pyrimidine portion of the Okada reference corresponds to "B" of compounds of Formula I of the present invention. See reference compound RN157911-86-9.

As amended, "B" of compounds of the present invention is limited to aryl, furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl and pyridazinyl. Therefore, the compounds discussed in the Okada reference do not anticipate the claims of the present invention.

The Barton Reference

Claims 1-5 also stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Barton et al. (*J. Am. Chem. Soc.*, 1993) (the "Barton reference").

The compound referred to in the Office Action having RN 150772-86-4P comprises a trifluoromethyl group attached to the nitrogen atom. See the CAS report provided by the Examiner. This trifluoromethyl group corresponds to R^1 of compound of Formula I of the present invention.

Unlike the Barton reference, substituent R^1 of compounds of the present invention can not be a trifluoromethyl group. In the present invention R^1 is limited to alkyl, alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl and alkylcarbonylalkyl.

Therefore, compounds of the present invention are not anticipated by the Barton reference.

In light of the above discussion, Applicants respectfully submit that that all of the stated rejections under 35 U.S.C. §102(b) are improper. Applicants hereby request that the rejection under 35 U.S.C. §102(b) be withdrawn.

Rejection under 35 U.S.C. §103

Claims 1, 2, 12, 13, and 43 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 4,857,530, issued to Berman et al. (the "Berman patent"). Specifically, the Office Action alleges that the Berman patent teaches a generic group of compounds which embraces compounds which are claimed in the present application. In support of this proposition, the Office Action then directs Applicants' attention to "formula I, Col. 2 wherein Ar is phenyl substituted with R^6 wherein R^6 is SO_2R^3...." The crux of the Examiner rejection of these claims is the premise that prior art disclosure of a genus renders *prima facie* obvious a species falling within the genus.

As discussed above, the aromatic group of the Berman patent (corresponding to "B" of Formula I) is a 4-oxo-quinazolinyl moiety , whereas "B" of Formula I of the present application is limited to aryl, furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl.

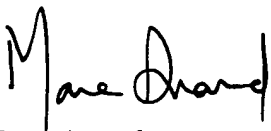
Furthermore, the compounds of the Berman patent have selective inhibitory activity against TS which in turn inhibits the growth of malignant neoplasms in mammals. The compounds of the present invention are anti-inflammatory and analgesic compounds and are prostglandin G/H synthase inhibitors. There is nothing in Berman to suggest, motivate or lead a person of ordinary skill in the art to reasonably expect that modifying the aromatic group of Berman patent ("B" in the present invention) will lead to the claimed compounds which are prostglandin G/H synthase inhibitors.

Applicants respectfully submit that Claims Claims 1, 2, 12, 13, and 43 are patentable over the Berman patent and request that the rejections under 35 U.S.C. §103 be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe Claims 1-19 and 38-43 now pending in this Application are in condition for allowance and request a Notice of Allowance for the same.

Respectfully submitted,



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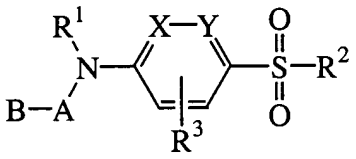
February 26, 2002

APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 1 has been amended as follows:

1. (Amended Herein) A compound ~~selected from the group of compounds represented by~~ **of** formula (I):



Formula I

wherein:

A is $-(CR_2)_n-$ where n is 1, 2 or 3 and R is independently hydrogen or alkyl;

B is aryl**, furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl** ~~or heteroaryl~~;

X and Y are, independently, CH or nitrogen;

R^1 is alkyl, alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl or alkylcarbonylalkyl;

R^2 is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, or $NR^{13}R^{14}$ wherein:

R^{13} is hydrogen or alkyl;

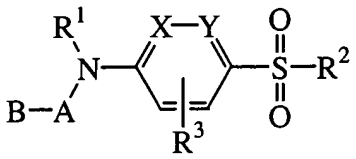
R^{14} is hydrogen, alkyl, aklenyl, acyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aralkyl, hydroxyalkyl, alkoxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, or aminoalkyl;

R^3 is hydrogen, alkyl, halo, nitro, cyano, hydroxy, alkoxy; ~~and~~ **or**

prodrugs, individual isomers, mixtures of isomers, **or** pharmaceutically acceptable salts thereof.

APPENDIX B
Pending Claims 1-19 and 38-43

1. (Amended Herein) A compound of the formula (I):



Formula I

wherein:

A is $-(CR_2)_n-$ where n is 1, 2 or 3 and R is independently hydrogen or alkyl;

B is aryl, furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl or pyridazinyl;

X and Y are, independently, CH or nitrogen;

R^1 is alkyl, alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl or alkylcarbonylalkyl;

R^2 is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, or $NR^{13}R^{14}$ wherein:

R^{13} is hydrogen or alkyl;

R^{14} is hydrogen, alkyl, aklenyl, acyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aralkyl, hydroxyalkyl, alkoxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, or aminoalkyl;

R^3 is hydrogen, alkyl, halo, nitro, cyano, hydroxy, alkoxy; or

prodrug, individual isomers, mixtures of isomers or pharmaceutically acceptable salt thereof.

2. The compound of Claim 1, wherein:

R^3 is hydrogen; and

X and Y are both CH.

3. The compound of Claim 2 wherein B is aryl.

4. The compound of Claim 3 wherein B is optionally substituted phenyl.

5. The compound of Claim 4 wherein R^1 is alkyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclylalkyl or heteroalkyalkyl.

6. The compound of Claim 5 wherein R^1 is heteroalkyl.

7. The compound of Claim 6 wherein R^1 is alkylsulfonylalkyl.

8. The compound of Claim 7 wherein R^2 is alkyl.

9. he compound of Claim 8 wherein A is $-(CH_2)-$.

10. The compound of Claim 7 wherein R^2 is $NR^{13}R^{14}$ wherein R^{13} and R^{14} are hydrogen.

11. The compound of Claim 10 wherein A is $-(CH_2)-$.

12. The compound of Claim 2 wherein B is heteroaryl.

13. The compound of Claim 12 wherein R^1 is alkyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclylalkyl or heteroalkyl.

14. The compound of Claim 13 wherein R^1 is heteroalkyl.

15. The compound of Claim 14 wherein R^1 alkylsulfonylalkyl.

16. The compound of Claim 15 wherein R^2 is alkyl.

17. The compound of Claim 16 wherein A is $-(CH_2)-$.

18. The compound of Claim 15 wherein R^2 is $NR^{13}R^{14}$ wherein R^{13} and R^{14} are hydrogen.

19. The compound of Claim 18 wherein A is $-(CH_2)-$.

38. The compound of Claim 1 wherein:
R^1 is alkylsulfonylalkyl;
B is aryl; and
X and Y are CH.

39. The compound of Claim 38, wherein R^2 is alkyl.

40. The compound of Claim 39, wherein A is $-(CH_2)-$.

41. The compound of Claim 38, wherein R^2 is NH_2.

42. The compound of Claim 41, wherein A is $-(CH_2)-$.

43. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable excipient.

* * * * * * * * * *